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(54) IgA NEPHROPATHY-ASSOCIATED GENE

(57) This invention relates to a method for obtaining a novel gene from leukocytes of IgA nephropathy patients, which uses a differential display method, and to diagnostic and therapeutic agents for IgA nephropathy comprising an oligonucleotide based on the nucleotide sequence of the DNA of the present invention.

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Description

TECHNICAL FIELD

[0001] The present invention relates to an isolation of a novel gene and a process for isolating the gene according to a differential display method taking note of an mRNA whose expression level fluctuates in leukocytes of IgA nephropathy patients in comparison with leukocytes of healthy persons. Also, the present invention relates to a novel protein, an antibody recognizing the protein, a DNA encoding the protein, a method for detecting the protein and the DNA, and diagnosis and treatment of IgA nephropathy.

BACKGROUND ART

[0002] IgA nephropathy is a chronic nephropathy which is characterized in that an IgA immune complex considered to be originated from blood deposits in glomerulus of the kidney. In Japan, the IgA nephropathy occupies 30% or more of primary renal diseases, and is the most common renal disease. Moreover, 15 to 30% of the patient with IgA nephropathy achieve renal failure due to poor prognosis. However, since the underlying cause of IgA nephropathy is still unclear, a fundamental therapeutic method has not been found. Additionally, definite diagnosis of IgA nephropathy imposes heavy burden on patients, because the method is carried out by removing a portion of the kidney by biopsy and recognizing deposition of the IgA immune complex in mesangium by means of an immunological staining.

[0003] It has been reported that about 50% of the patients with IgA nephropathy have a high blood IgA level [*Diseases of the Kidney*, 5th edition (1993), *Nephron*, 29, 170 (1981)]. It is considered that B cells relate to the production of IgA in blood and T cells relate to the regulation of the production. Furthermore, it has been reported that the production of cytokine, such as interleukin 4, interleukin 5, interleukin 6 or TGF-β (transforming growth factor-β), is high in peripheral T cells of IgA nephropathy patients in comparison with healthy persons [*Clinical & Experimental Immunology*, 103, 125 (1996), *Kidney International*, 46, 862 (1994))] and that integrin, such as VLA (very late activation)-4 and VLA-5, are strongly activated in peripheral lymphocytes of IgA nephropathy patients [*Nephrology, Dialysis, Transplantation*, 10, 1342 (1995)]. On the basis of these facts, it is considered that, in IgA nephropathy, excessive IgA is produced due to abnormality in the immune system, the resulting IgA immune complex in blood deposits on the glomerulus, and the complement system is activated on the deposited IgA immune complex and the like to exert influence and cause disorders of the glomerulus. However, the cause of IgA nephropathy has not yet been determined.

DISCLOSURE OF THE INVENTION

[0004] Elucidation of the cause of IgA nephropathy, as well as a treatment or diagnosis which can reduce a burden on patients are long-sought. The present invention provides a novel DNA related to IgA nephropathy, a method for isolating the DNA, a novel protein related to IgA nephropathy, an antibody recognizing the protein, a DNA encoding the protein, and a therapeutic drug and a diagnostic drug using them.

[0005] The present invention relates to a DNA related to IgA nephropathy gene, comprising the nucleotide sequence represented by SEQ ID NO:1 to NO: 31; and a DNA which hybridizes with said DNA under stringent conditions. The present invention relates to a method for detecting mRNA of an IgA nephropathy-related gene using an oligonucleotide based on the partial fragment of the DNA of the present invention and the nucleotide sequence complementary to the DNA; and an IgA nephropathy diagnostic agent comprising the oligonucleotide. The present invention relates to a method for inhibiting transcription of an IgA nephropathy-related gene or translation of the mRNA comprising using an oligonucleotide based on the partial fragment of the DNA of the present invention and the nucleotide sequence complementary to the DNA; and an IgA nephropathy therapeutic agent comprising the oligonucleotide. The present invention relates to a method for isolating an IgA nephropathy gene from leukocytes of a patient with IgA nephropathy comprising conducting a differential display method.

[0006] Furthermore, the present invention relates to a protein comprising the amino acid sequences represented by SEQ ID NO: 32; a DNA encoding the protein; a DNA comprising the nucleotide sequence represented by SEQ ID NO: 1; and a DNA which hybridizes with said DNA under stringent conditions. Moreover, the present invention relates to a recombinant DNA comprising the DNA and a vector; a transformant obtained by introducing the recombinant DNA into a host cell; and a method for producing a protein, comprising the steps of culturing the transformant in a medium to produce and accumulate a protein in the culture; and recovering the protein from the resulting culture. Also, the present invention relates to an antibody which recognizes the protein of the present invention; a method for immunologically detecting the protein comprising using the antibody; an IgA nephropathy diagnostic agent comprising the antibody; and an IgA nephropathy therapeutic agent comprising the antibody.

[0007] In the present invention, in order to obtain a novel gene, the differential display method [*FEBS Letters*, 351, 231 (1994)] which takes note of the difference in the expression quantity of mRNA in leukocytes between patients with

IgA nephropathy and healthy persons is used. The differential display method is a method in which cloning of a novel gene is carried out using pattern of manifestation as an index. That is, an amplified cDNA fragment of a novel gene whose expression level increases or decreases significantly in leukocytes of a patient with IgA nephropathy as compared with leukocytes of a healthy person is obtained by subjecting total RNA or mRNA extracted from cells to the polymerase chain reaction (PCR) using various primers. This method is described below.

[0008] Examples of the method for the preparation of a total RNA from leukocytes of patients with IgA nephropathy and leukocytes of healthy persons include guanidine thiocyanate-cesium trifluoroacetate method [*Methods in Enzymol.*, 154, 3 (1987)], the AGPC method [(*Jikken Igaku*, 9, 1937 (1991)], RNAeasy kit for recovering RNA (produced by QIAGEN), and the like.

[0009] Examples of the method for preparing poly(A)$^+$ RNA from the total RNA include oligo(dT)-immobilized cellulose column method (*Molecular Cloning, A Laboratory Manual*, 2nd ed.) and the like. Also, examples of the kit for preparing mRNA from leukocytes of patients with IgA nephropathy and leukocytes of healthy persons include Fast Track mRNA Isolation Kit (manufactured by Invitrogen), Quick Prep mRNA Purification Kit (manufactured by Pharmacia), and the like.

[0010] Using an anchor primer, cDNA is synthesized in the usual way from the RNA extracted by the above-described method from leukocytes of a patient with IgA nephropathy or leukocytes of a healthy person, and PCR is carried out using an anchor primer having a 5'-end labeled with fluorescence and an arbitrary primer. The anchor primer is a primer in which an oligonucleotide of adenine, guanine or cytosine, excluding thymidine, is added to the 3'-end of an oligo(dT) sequence which hybridizes with a 3'-end poly(A) sequence of mRNA. The arbitrary primer is an oligonucleotide which amplifies various cDNA sequences and can yield a large number of amplified cDNA fragments by a single reaction. Preferably, the oligonucleotide has a length of about 10 mer.

[0011] After the PCR, each of the amplified cDNA is subjected to polyacrylamide gel electrophoresis, and the fluorescence is detected with a fluorimager. By comparing the electrophoresis patterns of the amplified cDNA fragments derived from leukocytes of a patient with IgA nephropathy, the cDNA fragment in which the expression amplification is fluctuated is cut from the gel, the amplified cDNA fragment is inserted into a vector, and the nucleotide sequence of the DNA is determined by a usually used nucleotide sequence analyzing method such as the dideoxy method of Sanger *et al.* [*Proc. Natl. Acad. Sci. USA*, 74, 5463 (1977)], or the like.

[0012] Examples of the vector to which the DNA fragment is inserted include pDIRECT [*Nucleic Acids Research*, 18, 6069 (1990)], pCR-Script Amp SK(+) [manufactured by Stratagene, *Strategies*, 5, 6264 (1992)], pT7Blue (manufactured by Novagen), pCR II [manufactured by Invitrogen, *Biotechnology*, 9, 657 (1991)], pCR-TPAP (manufactured by Genehunter), pNoTA$_{T7}$ (manufactured by 5'→3') and the like.

[0013] The analysis of the nucleotide sequence is carried out by using a nucleotide sequence automatic analyzer, such as 373A • DNA sequencer (manufactured by Applied Biosystems), and the like.

[0014] The DNA of the present invention includes a DNA comprising the nucleotide sequence represented by SEQ ID NO:1 to NO: 31; a DNA which hybridizes with said DNA under stringent conditions; and the like.

[0015] Furthermore, the DNA which hybridizes under stringent conditions with a DNA comprising the nucleotide sequence represented by SEQ ID NO:1 to NO:31 means a DNA in which a mutation, such as substitution, deletion, incorporation, addition and the like, is introduced into at least one portion within the range that the inherent activities of the protein are not lost, and a DNA which is obtained by colony hybridization or plaque hybridization [*Molecular Cloning, A Laboratory Manual*, Second Edition (edited by Sambrook, Fritsch and Maniatis, Cold Spring Harbor Laboratory Press (1989)) (referred to as "*Molecular Cloning, A Laboratory Manual*, 2nd ed." hereinafter) using, as a probe, a DNA comprising a nucleotide sequence represented by SEQ ID NO:1 to NO: 31 or a fragment thereof.

[0016] Examples of a method for detecting the mRNA related to IgA nephropathy using the oligonucleotide based on the nucleotide sequence of the DNA of the present invention include Northern hybridization [*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press (1989)], PCR [*PCR Protocols*, Academic Press (1990)], and the like. Particularly, RT (Room Temperature)-PCR is simple and easy and can therefore be applied to the diagnosis of IgA nephropathy. Specifically, the amplified fragment is detected by collecting blood from human to recover leukocyte, transforming the RNA isolated therefrom into cDNA using an oilgo(dT) primer and a reverse transcriptase into, and conducting PCR using a pair of oligonucleotide primers corresponding to the mRNA to be detected.

[0017] Examples of the oligonucleotide primers include a sense primer corresponding to the 5'-end side nucleotide sequence, and an antisense primer corresponding to the 3'-end side nucleotide sequence, of a portion of the mRNA to be detected. In this case, the base corresponding to uracil in mRNA corresponds to thymidine in the oligonucleotide primer.

[0018] As the sense primer and antisense primer, it is preferred to use oligonucleotides in which melting point (T_m) and the number of bases are not significantly different from each other. Preferably, the base number is 15 to 40 mer.

[0019] The nucleotide sequence moiety to be amplified using the above oligonucleotide primer may be any nucleotide sequence region of the mRNA, but a nucleotide sequence region which has a length of 50 bp to 2 kbp and does not contain a sequence rich in a repeating sequence or GC (guanine-cytosine) bases is preferred.

[0020] Furthermore, similarly, the IgA nephropathy can be treated by inhibiting the transcription of DNA or translation of mRNA using an antisense RNA/DNA [*Chemistry*, 46, 681 (1991), *Biotechnology*, 9, 358 (1992)].

[0021] The inhibition of production of the protein using anti-sense RNA/DNA technology can be carried out by designing and preparing an oligonucleotide based on the nucleotide sequence of a portion of the DNA encoding the protein of the present invention, preferably that of 10 to 50 bases positioned in the translation initiation domain, and administrating it *in vivo*. As the nucleotide sequence of the synthesis oligonucleotide, those which partially conforms the nucleotide sequence of the anti-sense chain of the DNA encoding the protein of the present invention, or those which have been modified to the extent not to lose the activity of inhibiting the expression of the protein activity can be used. As oligonucleotide, DNA, RNA or their derivatives, such as methyl or phosphorothioate derivatives, can be used.

[0022] In order to obtain a full-length DNA from cDNA fragments obtained by the above-described method, screening from various cDNA libraries can be carried out by means of hybridization using the above-described amplified cDNA fragments as a probe. The method for preparing a cDNA library is described below.

[0023] Examples of the method for the preparation of the cDNA library include methods described in *Molecular Cloning, A Laboratory Manual*, 2nd. ed., or *Current Protocols in Molecular Biology, Supplement 1 to 34*, methods using a commercially available kit, such as Super Script™ Plasmid System for cDNA Synthesis and Plasmid Cloning (manufactured by Life Technologies) or ZAP-cDNA Synthesis Kit (manufactured by Stratagene), and the like. Additionally, several cDNA libraries are commercially available, including a cDNA library which can be used in the present invention such as a human leukocyte cDNA library manufactured by Gibco BRL and the like.

[0024] In the preparation of the cDNA library, the vector to which the cDNA, synthesized using mRNA extracted from cell as a template, is inserted may be any vector so long as the cDNA can be inserted thereto. Examples include ZAP Express [*Strategies*, 5, 58 (1992)], pBluescript II SK(+) [*Nucleic Acids Research*, 17, 9494 (1989)], λ zap II (manufactured by Stratagene), λgt10, λgt11 [*DNA Cloning, A Practical Approach*, 1, 49 (1985)], Lambda BlueMid (manufactured by Clonetech), λExCell, pT7T318U (manufactured by Pharmacia), pcD2 [*Mol. Cell. Biol.*, 3, 280 (1983)], pUC18 [*Gene*, 33, 103 (1985)], and the like. With regard to the *Escherichia coli* for introducing the cDNA library constituted by the vector, any microorganism belonging to *Escherichia coli* can be used so long as the introduction, expression and maintenance of the cDNA library can be conducted. Examples include *Escherichia coli* XL1-Blue MRF' [*Strategies*, 5, 81 (1992)], *Escherichia coli* C600 [*Genetics*, 39, 440 (1954)], *Escherichia coli* Y1088, *Escherichia coli* Y1090 [*Science*, 222, 778 (1983)], *Escherichia coli* NM522 [*J. Mol. Biol.*, 166, 1 (1983)], *Escherichia coli* K802 [*J. Mol. Biol.*, 16, 118 (1966)], *Escherichia coli* JM105 [*Gene*, 38, 275 (1985)], and the like.

[0025] The cDNA can be also obtained without preparing a cDNA library by the 5'-RACE (rapid amplification of cDNA ends) and 3'-RACE [*Proc. Natl. Acad. Sci. USA*, 85, 8998 (1988)] in which adapters are added to both ends of the cDNA and then PCR is carried out using primers based on the nucleotide sequence of the adapter and the nucleotide sequence of the amplified fragment. Alternatively, the cDNA can be obtained by PCR based on the nucleotide sequence or a chemical synthesis method using a DNA synthesizer. A cDNA clone can be selected from the cDNA library according to a colony hybridization or plaque hybridization method (*Molecular Cloning, A Laboratory Manual*, 2nd ed.) using a probe labeled with an isotope or fluorescence. The cDNA may be also prepared according to the polymerase chain reaction (PCR) (*Molecular Cloning, A Laboratory Manual*, 2nd ed. or *Current Protocols in Molecular Biology, Supplement 1 to 34*) by preparing a primer and using, as a template, cDNA synthesized from poly (A)$^+$RNA or mRNA, or cDNA library.

[0026] The nucleotide sequence of the DNA can be determined by cleaving the cDNA clone selected by the above method with an appropriate restriction enzyme, cloning to a plasmid, such as pBluescript KS(+) (manufactured by Stratagene) or the like, and then analyzing by a conventional nucleotide sequence analysis method, such as dideoxy method of Sanger *et al.* [*Proc. Natl. Acad. Sci., U.S.A.*, 74, 5463 (1977)] or the like. The nucleotide sequence can be analyzed by using a nucleotide sequence automatic analyzer, such as 373A • DNA sequencer (manufactured by Applied Biosystems) or the like.

[0027] Confirmation of novelty of the thus obtained nucleotide sequence is carried out using nucleotide sequence data bases, such as GenBank, EMBL, DDBJ, and the like.

[0028] Examples of the DNA obtained by the above-described method include a DNA comprising the nucleotide sequence represented by SEQ ID NO:1 and a DNA which hybridizes with said DNA under stringent conditions. Also, examples of the protein comprising an amino acid sequence deduced from said nucleotide sequence include a protein comprising the amino acid sequence represented by SEQ ID NO:32.

[0029] The preparation and expression of the DNA encoding the novel protein of the present invention is carried out according to the process described in *Molecular Cloning, A Laboratory Manual*, 2nd ed., *Current Protocols in Molecular Biology, Supplement 1 to 34* (edited by Ausubel, Brent, Kingston, Moore, Seidman, Smith and Struhl, published by Green Publishing Associates and Wiley-Interscience, 1987-1996 edition) (referred to as "*Current Protocols in Molecular Biology, Supplement 1 to 34*"), and the like.

[0030] A transformant which expresses the protein of the present invention can be obtained by preparing a transformed vector to which the full-length DNA prepared according to the above method is inserted into a downstream site

of the promoter in an appropriate vector.

[0031] As the host cell, any bacterium, yeast, animal cell, insect cell, and the like, can be used so long as they can express the gene of interest. Examples of the bacterium include bacteria belonging to the genus *Escherichia, Serratia, Corynebacterium, Brevibacterium, Pseudomonas, Bacillus,* and the like, for example, *Escherichia coli, Bacillus subtilis, Bacillus amyloliquefaciens, Brevibacterium flavum, Brevibacterium lactofermentum, Corynebacterium glutamicum, Microbacterium ammoniaphilum,* and the like. Examples of the yeast include *Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces lactis, Trichosporon pullulans, Schwanniomyces alluvius* and the like. Examples of the animal cell include human Namalwa cell, monkey COS cell, Chinese hamster CHO cell, and the like. Examples of the insect cell include *Spodoptera frugiperda* oocytes Sf9 and Sf21 [*Bacurovirus Expression Vectors, A Laboratory Manual,* Oreilly, Miller and Luckow, W.H. Freeman and Company, New York, (1992) (referred to as "*Bacurovirus Expression Vectors, A Laboratory Manual*" hereinafter)], *Trichoplusia ni* oocyte Tn5 (High 5, manufactured by Pharmingen), and the like.

[0032] Any vector can be used as the vector to which the DNA of the present invention is inserted so long as it can introduce the DNA and drive the expression in the host cell.

[0033] When a bacterium, such as *Escherichia coli*, is used as the host cell, it is preferred that the vector is constituted by a promoter, a ribosome binding sequence, the DNA of the present invention and a transcription termination sequence. A promoter controlling gene may be also contained.

[0034] Examples of the expression vector include pKYP10 (Japanese Published Unexamined Patent Application No. 110600/83), pLSA1 [*Agric. Biol. Chem.*, 53, 277 (1989)], pGEL1 [*Proc. Natl. Acad. Sci. USA*, 82, 4306 (1985)], and the like.

[0035] With regard to the promoter, any promoter can be used so long as it can drive the expression in the host cell. Examples include promoters originated from *Escherichia coli*, phage and the like (for example, *trp* promoter (P*trp*), *lac* promoter (P*lac*), T7 *lac* promoter, PL promoter, PR promoter, and the like). Also, artificially designed and modified promoters, such as a promoter in which two P*trp* are linked in series (P*trp* × 2), *tac* promoter, and the like, can be used.

[0036] With regard to the ribosome binding sequence, it is preferred to use a plasmid in which the space between Shine-Dalgarno sequence (referred to as "SD sequence" hereinafter) and the initiation codon is adjusted to an appropriate distance (for example, 6 to 18 bases).

[0037] With regard to the recombinant vector of the present invention, it is preferred to substitute a suitable nucleotide in order that the nucleotide sequence of the DNA of the present invention forms a codon suitable for the expression of a host cell.

[0038] The transcription termination sequence is not always necessary for the recombinant vector of the present invention. However, it is preferred to arrange the transcription terminating sequence just downstream of the structural gene.

[0039] With regard to the method for the introduction of the recombinant vector to the bacterium, any one of the known methods for introducing DNA into the bacterium, such as a method in which calcium ion is used [*Proc. Natl. Acad. Sci. USA*, 69, 2110-2114 (1972)], a protoplast method (Japanese Published Unexamined Patent Application No. 2483942/88), and the like, can be used.

[0040] When yeast is used as the host cell, YEp13 (ATCC 37115), YEp24 (ATCC 37051), YCp50 (ATCC 37419), or the like is used as the expression vector.

[0041] Any promoter can be used so long as it can drive the expression in yeast. Examples include promoters of genes in the glycolysis system (for example, hexosekinase, and the like), gal 1 promoter, gal 10 promoter, heat shock protein promoter, MFα1 promoter, CUP 1 promoter and the like.

[0042] With regard to the method for the introduction of the recombinant vector, any one of known methods for introducing DNA into yeast, such as an electroporation method [*Methods. Enzymol.*, 194, 182-187 (1990)], a spheroplast method [*Proc. Natl. Acad. Sci. USA*, 84, 1929-1933 (1978)], a lithium acetate method [*J. Bacteriol.*, 153, 163-168 (1983)], and the like can be used.

[0043] When animal cells are used as the host cells, pAGE107 [Japanese Published Unexamined Patent Application No. 22979/91; *Cytotechnology*, 3, 133 (1990)], pAS3-3 (Japanese Published Unexamined Patent Application No. 227075/90), pAMoERC3Sc, pcDM8 [*Nature*, 329, 840 (1987)], pcDNAI/Amp, pcDNAI (both manufactured by Funakoshi), and the like can be exemplified as the expression vector.

[0044] Any promoter can be used so long as it can drive the expression in animal cell. Examples include a promoter of IE (immediate early) gene of cytomegalovirus (CMV), a promoter of SV40 or metallothionein, and the like. Also, the enhancer of the IE gene of human CMV may be used together with the promoter.

[0045] With regard to the method for the introduction of the recombinant vector into animal cells, any one of the known methods for introducing DNA into animal cells, such as an electroporation method [*Cytotechnology*, 3, 133 (1990)], a calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90), a lipofection method [*Proc. Natl. Acad. Sci. USA*, 84, 7413 (1987)], and the like can be used.

[0046] When an insect cell is used as the host cell, the protein can be expressed by known methods described in, for

example, *Current Protocols in Molecular Biology, supplement 1-34; Bacurovirus Expression Vectors, A Laboratory Manual*; or the like. That is, a recombinant gene transfer vector and bacurovirus are simultaneously introduced into an insect cell to obtain a recombinant virus in an insect cell culture supernatant, and then insect cells are infected with the thus obtained recombinant virus to obtain protein expression insect cell.

[0047] Examples of the gene transferring vector include pVL1392, pVL1393, pBlueBacIII (all manufactured by Invitrogen), and the like.

[0048] Examples of the bacurovirus include Autographa californica nuclear polyhedrosis virus with which insects of the family *Barathra* are infected, and the like.

[0049] The method for the co-transfer of the above-described recombinant gene transfer vector and the above-described bacurovirus for the preparation of the recombinant virus include a calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90), a lipofection method [*Proc. Natl. Acad. Sci. USA*, 84, 7413 (1987)], and the like.

[0050] The protein of the present invention can be produced by culturing the thus obtained transformant in a culture medium to produce and accumulate the protein of the present invention, and recovering the protein from the resulting culture.

[0051] Culturing of the transformant of the present invention in a culture medium is carried out in accordance with a usual method used in culturing of host cells.

[0052] The medium for culturing the transformant obtained by using as the host cell a microorganism, such as *Escherichia coli*, yeast or the like, may be either a natural medium or a synthetic medium, so long as it contains a carbon source, a nitrogen source, an inorganic salt and the like which can perform culturing of the transformant efficiently.

[0053] Examples of the carbon source include carbohydrates (for example, glucose, fructose, sucrose, molasses, starch, starch hydrolysate, and the like), organic acids (for example, acetic acid, propionic acid, and the like), and alcohols (for example, ethanol, propanol, and the like).

[0054] Examples of the nitrogen source include ammonia, various ammonium salts of inorganic acids or organic acids (for example, ammonium chloride, ammonium sulfate, ammonium acetate, ammonium phosphate, and the like), other nitrogen-containing compounds, peptone, meat extract, yeast extract, corn steep liquor, casein hydrolysate, soybean meal and soybean meal hydrolysate, various fermented cells and hydrolysates thereof, and the like.

[0055] Examples of inorganic substance include potassium dihydrogen phosphate, dipotassium hydrogen phosphate, magnesium phosphate, magnesium sulfate, sodium chloride, ferrous sulfate, manganese sulfate, copper sulfate, calcium carbonate, and the like.

[0056] The culturing is carried out under aerobic conditions by means of shaking, aeration stirring or the like at 15 to 45°C for 16 to 96 hours. The pH of the medium is maintained at 3.0 to 9.0 during the culturing. Adjustment of the medium pH is carried out using an inorganic or organic acid, an alkali solution, urea, calcium carbonate, ammonia and the like.

[0057] Also, antibiotics (for example, ampicillin, tetracycline, and the like) may be added to the medium during the culturing as occasion demands.

[0058] When a microorganism transformed with an expression vector containing an inducible promoter is cultured, an inducer may be added to the medium as occasion demands. For example, isopropyl-β-D-thiogalactopyranoside (IPTG) r the like may be added to the medium when a microorganism transformed with an expression vector containing *lac* promoter is cultured, or indoleacrylic acid (IAA) or the like may by added thereto when a microorganism transformed with an expression vector containing *trp* promoter is cultured.

[0059] Examples of the medium used in the culturing of a transformant obtained using an animal cell as the host cell include RPMI 1640 medium, Eagle's MEM medium, and any one of these media further supplemented with fetal calf serum. The culturing is carried out generally at a temperature of 35 to 37°C for a period of 3 to 7 days in the presence of 5% CO_2. As occasion demands, antibiotics (for example, kanamycin, penicillin, and the like) may be added to the medium during the culturing.

[0060] Examples of the medium used in the culturing of a transformant obtained using an insect cell as the host cell include TNM-FH medium (manufactured by Pharmingen), Sf900 II SFM (manufactured by Life Technologies), ExCell 400 or ExCell 405 (both manufactured by JRH Biosciences), and the like. The culturing is carried out generally at a temperature of 25 to 30°C for a period of 1 to 4 days. Additionally, antibiotics (for example, gentamicin, and the like) may be added to the medium during the culturing as occasion demands.

[0061] When the protein of the present invention is expressed in a dissolved state inside the cells, or when it forms an inclusion body, the cells after completion of the culturing are recovered by centrifugation, suspended in an aqueous buffer and then disrupted by ultrasonic, French press or the like to btain the protein from a supernatant fluid prepared by centrifugation.

[0062] Also, when the protein forms an inclusion body, the inclusion body is solubilized using a protein denaturing agent, and then the solubilized solution is diluted to or dialyzed against a solution containing no protein denaturing agent or a dilute solution containing a protein denaturing agent in such a concentration that the protein is not denatured

in order to form a renatured protein.

[0063] When the protein of the present invention or a derivative thereof, such as a sugar-modified product or the like, is secreted outside the cells, the protein or the derivative, such as a sugar-modified product or the like, can be recovered from the culture supernatant. That is, the isolation and purification can be conducted by using isolation steps, such as solvent extraction, fractional precipitation by an organic solvent, salting-out, dialysis, centrifugation, ultrafiltration, ion exchange chromatography, gel filtration chromatography, hydrophobic interaction chromatography, affinity chromatography, reverse phase chromatography, crystallization, electrophoresis, and the like, alone or as a combination thereof.

[0064] Furthermore, the protein of the present invention can be prepared according to a chemical synthesis method based on the amino acid sequence represented by SEQ ID NO:32.

[0065] The antibody can be produced by immunizing an animal using the protein of the present invention as an antigen or a peptide, chemically synthesized based on the amino acid sequence represented by SEQ ID NO: 32 which is a portion of the protein of the present invention. A monoclonal antibody to the protein of the present invention can be prepared by preparing a hybridoma through fusion of the antibody producing cells with myeloma cells of an animal and culturing the hybridoma, or administering the hybridoma to the animal to induce ascites tumor in the animal, and then isolating and purifying it from the culture medium or ascitic fluid. Also, a polyclonal antibody to the protein of the present invention can be prepared by isolating the immune serum of the immune animal. These antibodies can be used in the diagnosis and treatment of IgA nephropathy.

[0066] The examples of the present invention are shown below.

[EXAMPLES]

Example 1 Differential display of leukocytes of IgA nephropathy patients and healthy persons

(1) Preparation of total RNA from leukocytes of IgA nephropathy patients and healthy persons

[0067] A 20 ml portion of blood was collected from each of five IgA nephropathy patients and five healthy persons. This was mixed with 500 µl of 1,000 units/ml heparin sodium solution (manufactured by Shimizu Seiyaku) to inhibit coagulation, transferred into a centrifugation tube and then centrifuged at 3,300 rpm for 15 minutes at room temperature, and the resulting intermediate layer buffy coat containing leukocytes was transferred into another centrifugation tube. Thereafter, total RNAs were obtained in accordance with the AGPC method [*Experimental Medicine*, 9, 1937 (1991)] or using an RNA recovering kit RNAeasy (manufactured by QIAGEN).

(2) Fluorescence differential display using leukocyte total RNAs of IgA nephropathy patients and healthy persons

[0068] Distilled water was added to 2.5 µg of each of the total RNAs to a total volume of 9 µl, and the solution was mixed with 1 µl of an anchor primer (50 µM, custom-synthesized by Sawady) whose 5'-end had been fluorescence-labeled with fluorescein isothiocyanate (referred to as "FITC" hereinafter), heated at 70°C for 5 minutes and then immediately cooled on an ice bath. Since each of the three primers FAH (FAH: 5'-FITC-GT_{15}A-3'), FGH (FGH: 5'-FITC-GT_{15}G-3') and FCH (FCH: 5'-FITC-GT_{15}C-3') was used in each reaction as the fluorescence-labeled anchor primer, a total of three combinations of reactions were carried out for one sample of total RNAs. A 4 µl portion of 5 × reverse transcriptase reaction buffer [250 mM tris(hydroxymethyl)aminomethane (Tris)-HCl (pH 8.3), 375 mM KCl, 15 mM $MgCl_2$] was mixed with 2 µl of 100 mM dithiothreitol (DTT), 1 µl of 10 mM dNTP (dATP, dGTP, dTTP and dCTP), 1 µl of distilled water and 1 µl (200 units) of a reverse transcriptase SUPERSCRIPT II RNase H$^-$ Reverse Transcriptase (manufactured by BRL), and the resulting mixture was allowed to stand at room temperature for 10 minutes, allowed to react at 42°C for 50 minutes to synthesize a cDNA, and then heated at 90°C for 5 minutes to terminate the reaction. To the reaction solution was added 40 µl of TE buffer [10 mM Tris-HCl (pH 8.0), 1 mM disodium ethylenediamine-tetraacetate (EDTA) (pH 8.0)].

[0069] Subsequently, next, 14.7 µl of distilled water, 2 µl of 10 × PCR buffer [100 mM Tris-HCl (pH 8.8), 500 mM KCl, 15 mM $MgCl_2$, 1% Triton X-100], 0.8 µl of 2.5 mM dNTP, 0.3 µl of 50 µM fluorescence-labeled anchor primer (the same among FAH, FGH and FCH used in the cDNA synthesis), 1 µl of 10 µM arbitrary primer (manufactured by Operon) and 0.2 µl of DNA polymerase Gene Taq (5 units/µl, manufactured by Nippon Gene) were added to 1 µl of each of the thus synthesized cDNA samples, and the resulting mixture was arranged in Thermal Cycler. The PCR was effected by carrying out the reaction at 94°C for 3 minutes, 40°C for 5 minutes and 72°C for 5 minutes, subsequently carrying out a total of 27 cycles of the reaction in which one cycle was comprised of the steps of 95°C for 15 seconds, 40°C for 2 minutes and 72°C for 1 minute, and finally carrying out 5 minutes of the reaction at 72°C. Since each reaction was carried out by a combination of one of the above-described three types as the fluorescence-labeled anchor primer with one of 60 types of OPD-1 to 20, OPE-1 to 20 and OPV-1 to 20 manufactured by Operon as the arbitrary primer, a total of 180 reactions, and since a reaction of the fluorescence-labeled anchor primer FGH with an arbitrary primer OPB-2 (manu-

factured by Operon) was also carried out, a total of 181 reactions were carried out for the total RNAs.

[0070] A 4 μl portion of each of the PCR reaction solutions was mixed with 3 μl of electrophoresis sample buffer use (95% formamide, 0.1% xylene cyanol, 0.1% Bromophenol Blue), and the mixture was heated at 95°C for 2 minutes, immediately cooled thereafter on an ice bath and then subjected to 2.5 hours of 6% acrylamide gel electrophoresis at 1,500 V. A solution composed of 89 mM Tris, 89 mM boric acid and 2 mM EDTA was used as the electrophoresis buffer. By measuring fluorescence of the gel after electrophoresis using Fluorimager (manufactured by Molecular Dynamics), the fragments amplified by PCR were detected and compared. In comparison with 5 cases of the healthy persons, a band which significantly increased or decreased in leukocytes of 5 cases of the IgA nephropathy patients was recorded.

[0071] Total RNAs were prepared from other 3 cases of IgA other nephropathy patients and 3 cases of other healthy persons in the same manner to carry out the differential display in the same manner. A total of 197 bands which showed increased or decreased fluorescence in both of the above two trials of the differential display were cut off from the gels.

[0072] A 38 μl portion of distilled water, 5 μl of 10 × PCR buffer, 4 μl of 2.5 mM dNTP, 0.6 μl of an anchor primer (no fluorescence labeling: 34 μM, custom-synthesized by Sawady), 2 μl of 10 μM arbitrary primer and 0.5 μl of DNA polymerase Gene Taq were added to about 1/4 portion of each of the gels thus cut off, the resulting mixture was heated at 94°C for 3 minutes and then a total of 30 cycles of the reaction was carried out in which one cycle was comprised of the steps of 95°C for 15 seconds, 40°C for 2 minutes and 72°C for 1 minute, subsequently carrying out 5 minutes of the reaction at 72°C to complete PCR. The same combinations of anchor primers with optional primers used in the first differential display method were employed. Each of the resulting reaction solutions was extracted with phenol-chloroform (1:1) and then with chloroform-isoamyl alcohol (24:1), subsequently carrying out ethanol precipitation. To purify the precipitate, 1.5% low melting point agarose gel (SEA PLAQUE GTG, manufactured by FMC Bioproducts) electrophoresis was carried out. After the electrophoresis, the resulting gels were stained with ethidium bromide and then the bands containing amplified fragments were cut off. The gel was heated at 65°C for 15 minutes to melt agarose and then extracted with phenol-chloroform. After chloroform-isoamyl alcohol extraction, the thus obtained extract was subjected to ethanol precipitation and the resulting precipitate was dissolved in 10 μl of TE buffer.

[0073] A 1 μl portion of each of the amplified fragments was mixed with 1 μl of a vector for PCR fragment cloning use, pT7BlueT-Vector (manufactured by Novagen), and the amplified fragment was cloned into the plasmid using DNA Ligation Kit ver.1 (manufactured by Takara Shuzo) in accordance with the manual attached to the kit. *Escherichia coli* DH5α (manufactured by Gibco BRL) was transformed in accordance with a known method, and the ampicillin-resistant transformant was obtained. The transformant colony was suspended in 20 μl of distilled water, the suspension was mixed with 2.5 μl of 10 × PCR buffer, 2 μl of 2.5 mM dNTP, 0.3 μl of 34 μM anchor primer, 1 μl of 10 μM arbitrary primer and 0.5 μl of a DNA polymerase Gene Taq, and the mixture was subjected to PCR under the same conditions of the above-described re-amplification of amplified fragments and then analyzed by electrophoresis which recognized that an amplified fragment has the same length as in the first differential display, and therefore, the amplified fragment was cloned into the plasmid.

[0074] Nucleotide sequence of the amplified fragment was determined using DNA Sequencer (manufactured by Perkin Elmer). In carrying out the nucleotide sequence determination, Dye Primer Cycle Sequencing Kit manufactured by Perkin Elmer and the method described in the manual attached to the kit were used. Using restriction enzymes capable of cleaving restriction enzyme sites in the determined nucleotide sequence, the reaction product obtained by the above-described differential display was cleaved and then subjected to electrophoresis to recognize that the position of electrophoresis band corresponding to the thus cut off amplified fragment was changed. Each of the thus obtained nucleotide sequences was compared with a nucleotide sequence data base GenBank to select a total of 66 clones which were not present among the known nucleotide sequences in the data base or coincided only with the expressed sequence tag among nucleotide sequences in the data base.

Example 2 Detection of specificity of mRNA expression by RT-PCR

[0075] Using 2 μg of each of the total RNA samples obtained in Example 1 from leukocytes of five cases of IgA nephropathy patients and 5 cases of healthy persons, single-stranded cDNA was synthesized using a single-stranded cDNA synthesis kit Superscript Preamplification System (manufactured by BRL) by the oligo(dT) primer attached to the kit. Specific reagents and method employed were as described in the protocol attached to the kit. A 21 μl portion of solution after the reaction was adjusted to a total volume of 420 μl by adding 399 μl of distilled water, and a 10 μl portion of the thus prepared solution was used in the detection of the expression quantity of mRNA corresponding to each amplified fragment by RT-PCR. That is, 10 μl of the leukocyte single-stranded cDNA solution was mixed with 15.8 μl of distilled water, 4 μl of 10 × PCR buffer, 3.2 μl of 2.5 mM dNTP, 2 μl of DMSO, 2 μl of 10 μM gene-specific 5'-end side sense primer, 2 μl of 10 μM gene-specific 3'-end side antisense primer and 2 μl of a DNA polymerase Gene Taq which had been diluted to 1 unit/μl, and the resulting mixture was heated at 94°C for 5 minutes, cooled on an ice bath for 5 minutes and then subjected to a total of 24 to 35 cycles of PCR in which one cycle was comprised of the steps of 95°C for 30 seconds, 65°C for 1 minute and 72°C for 2 minutes. After carrying out 2% agarose gel electrophoresis, the gel was

stained with 0.01% Cyber Green (manufactured by Takara Shuzo), and the amount of the amplified fragment determined by Fluorimager was used as relative expression quantity of mRNA.

[0076] In order to make a correction of the amount of mRNA, the same reaction was carried out on a housekeeping gene, glyceraldehyde 3-phosphate dehydrogenase (G3PDH) gene, using specific primers (5'-CCCATCACCATCTTCCAGGAGC-3', 5'-TTCACCACCTTCTTGATGTCATCATA-3') and the expression level of mRNA for each gene was corrected based on the ratio of the expression level of G3PDH mRNA, and then the average value of five cases of IgA nephropathy patients and the average value of 5 cases of healthy persons were compared and 31 gene clones having a difference in their values were selected as genes whose expression quantity was changed in patients with IgA nephropathy. The thus selected genes are summarized in Tables 1-1 and 1-2.

Table 1-1

SEQ ID NO	Gene	Amplification primer[1)]	bp[2)]	Expression fluctuation[3)]	RT-PCR primer[4)]	RT-PCR cycle number
1	INP377-A	FGH/OPD-1	256	5.0	55, 56	28
2	INM063-7	FGH/OPB-2	155	12.5	33, 34	28
3	INP303-A	FAH/OPD-5	305	9.9	35, 36	28
4	INM315-10	FAH/OPD-9	278	2.8	37, 38	35
5	INP319-3	FAH/OPD-10	135	14.4	39, 40	28
6	INP324-A	FAH/OPD-12	197	19.9	41, 42	28
7	INP332-A	FAH/OPD-16	137	16.6	43, 44	28
8	INM335-3	FAH/OPD-17	274	4.2	45, 46	28
9	INM336-A	FAH/OPD-17	171	0.14	47, 48	28
10	INM351-10	FCH/OPD-4	161	1.8	49, 50	28
11	INP356-4	FCH/OPD-7	323	18.5	51, 52	35
12	INP364-A	FCH/OPD-12	138	3.8	53, 54	28
13	INP379-A	FGH/OPD-2	244	8.6	57, 58	35
14	INP380-A	FGH/OPD-2	135	15.7	59, 60	35
15	INP401-A	FGH/OPD-20	258	16.7	61, 62	24
16	INM403-A	FAH/OPE-3	219	2.3	63, 64	28
17	INP407-A	FAH/OPE-5	191	9.1	65, 66	28
18	INM408-A	FAH/OPE-5	148	0.65	67, 68	28
19	INP410-5	FAH/OPE-6	306	2.0	69, 70	28
20	INM419-14	FAH/OPE-11	357	0.064	71, 72	35

1): A combination of the anchor primer with the arbitrary primer used in the differential display is shown.
2): The length of the amplified fragment of the differential display is shown, excluding GTINP332A-21.
3): Expression fluctuation is shown as the value of "the average value of mRNA expression levels in 5 cases of IgA nephropathy patients/the average value of mRNA expression levels in 5 cases of healthy persons".
4): The primer used in the RT-PCR is shown by the SEQ ID NO.

Table 1-2

21	INP429-A	FGH/OPE-7	219	2.4	73, 74	28
22	INP431-A	FGH/OPE-8	251	13.1	75, 76	24
23	INP438-A	FGH/OPE-11	233	5.4	77, 78	24
24	INP444-A	FGH/OPE-15	176	3.3	79, 80	24
25	INP451-2	FCH/OPE-4	241	14.0	81, 82	32
26	INP458-A	FCH/OPE-11	217	9.2	83, 84	28
27	INP463-A	FCH/OPE-19	232	18.2	85, 86	35
28	INP470-A	FCH/OPV-4	228	5.8	87, 88	28
29	INP482-A	FCH/OPV-10	298	9.9	89, 90	28
30	INP485-6	FCH/OPV-17	291	8.5	91, 92	28
31	GTINP332A-21[5)]	-	869	4.6	93, 94	24

5): GTINP332A-21 is not a gene from which its amplified fragment was obtained by the differential display, but is a cDNA clone obtained from a transformant when an attempt was made to obtain a cDNA clone of full-length length INP332-A from a human leukocyte cDNA library in the same manner as described in Example 3. This gene was included in this table, because, when a portion of its cDNA nucleotide sequence was determined in the same manner as described in Example 4, this was found to be a cDNA clone of a novel gene whose nucleotide sequence is different from that of INP332A, and the result of PCR carried out in Example 2 based on its nucleotide sequence showed that expression of mRNA was increased in leukocytes of IgA nephropathy patients in comparison with the case of healthy persons.

[0077] Thus, it becomes possible to carry out diagnosis of IgA nephropathy by observing the expression levels of these genes in the leukocytes samples to be tested by PT-PCR using primers of these genes and mRNAs of the samples.

Example 3 Cloning of whole length cDNA

(1) Isolation of INP377-A cDNA clone

[0078] A INP377-A cDNA clone was obtained from a human leukocyte cDNA library (manufactured by Gibco BRL) in which pCMV-SPORT (manufactured by Gibco BRL) was used as the vector, using GENE TRAPPER cDNA Positive Selection System (manufactured by Gibco BRL). That is, the clone of interest was isolated by making clones in the cDNA library into single-stranded chains using Gene II protein and exonuclease III, carrying out their hybridization with a probe, namely a biotinated complimentary oligonucleotide (the 5'-side sense primer used in Example 2 was used) which corresponds to the INP377-A gene, and then allowing the probe to bind to magnetic beads to which streptoavidin has been added. The thus hybridized single-stranded cDNA was released from the probe, made into double-stranded chain using a DNA polymerase and then transformed into *Escherichia coli*, thereby obtaining the INP377-A cDNA clone as an ampicillin resistant strain. Specific reagents and method employed were as described in the protocol attached to the kit. Each of the transformant colonies was suspended in 18 μl of distilled water, the suspension was mixed with 2.5 μl of 10 × PCR buffer, 2 μl of 2.5 mM dNTP, 1 μl of 10 μM gene-specific 5'-end side sense primer, 1 μl of 10 μM gene-specific 3'-end side antisense primer and 0.5 μl of a DNA polymerase Gene Taq, and the resulting mixture was subjected to PCR under the same conditions of RT-PCR, subsequently carrying out an electrophoresis to isolate a transformant as the INP377-A cDNA clone of interest in which an INP377-A cDNA fragment of about 200 bp deduced from the positions of primers was amplified.

[0079] Plasmid DNA was isolated from this clone in accordance with the known method (*Molecular Cloning: A laboratory manual*, 2nd ed.), and the plasmid was named pGTINP377A-46C. In addition, the plasmid DNA was digested with restriction enzymes *Sal*I and *Not*I (both manufactured by Takara Shuzo) and then subjected to agarose gel electrophoresis to find that the cDNA has a size of about 3 kb.

(2) Determination of INP377-A cDNA nucleotide sequence

[0080] Nucleotide sequence of INP377-A cDNA in pGTINP377A-46C was determined using 377 DNA Sequencer manufactured by Perkin-Elmer. With regard to specific reagents and method used in the nucleotide sequence determination, Dye Primer Cycle Sequencing FS Ready Reaction Kit manufactured by Perkin-Elmer was used in accordance with the instructions of the kit. The thus determined nucleotide sequence is shown in SEQ ID NO:1. An open reading frame (ORF) corresponding to 143 amino acids was present in this nucleotide sequence. When the 377-A cDNA nucleotide sequence was compared with a data base, it was found that its partial sequence corresponding to N-terminal 137 amino acids coincides with the partial sequence of the human gene LUCA15, which corresponds to N-terminal 137 amino acids having homology with a Drosophila cancer inhibition gene Sx1, but a nucleotide sequence having no homology continues thereafter, and the sequence obtained by the differential display is present in this nucleotide sequence having no homology.

INDUSTRIAL APPLICABILITY

[0081] IgA nephropathy can be diagnosed and treated by using the novel gene obtained according to the present invention.

SEQUENCE LISTING

SEQ ID NO:1
SEQUENCE LENGTH: 2689
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:

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AAAATTTGAA CCTTTTGGAG CTGTGTGCTA AATCTTCAGT GGGACA ATG GGT TCA        115
                                                    Met Gly Ser
                                                     1
GAC AAA AGA GTG AGT AGA ACA GAG CGT AGT GGA AGA TAC GGT TCC ATC       163
Asp Lys Arg Val Ser Arg Thr Glu Arg Ser Gly Arg Tyr Gly Ser Ile
  5                  10                  15
ATA GAC AGG GAT GAC CGT GAT GAG CGT GAA TCC CGA AGC AGG CGG AGG       211
Ile Asp Arg Asp Asp Arg Asp Glu Arg Glu Ser Arg Ser Arg Arg Arg
 20                  25                  30                  35
GAC TCA GAT TAC AAA AGA TCT AGT GAT GAT CGG AGG GGT GAT AGA TAT       259
Asp Ser Asp Tyr Lys Arg Ser Ser Asp Asp Arg Arg Gly Asp Arg Tyr
                 40                  45                  50
GAT GAC TAC CGA GAC TAT GAC AGT CCA GAG AGA GAG CGT GAA AGA AGG       307
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AAC AGT GAC CGA TCC GAA GAT GGC TAC CAT TCA GAT GGT GAC TAT GGT       355
Asn Ser Asp Arg Ser Glu Asp Gly Tyr His Ser Asp Gly Asp Tyr Gly
         70                  75                  80
GAG CAC GAC TAT AGG CAT GAC ATC AGT GAC GAG AGG GAG AGC AAG ACC       403
Glu His Asp Tyr Arg His Asp Ile Ser Asp Glu Arg Glu Ser Lys Thr
     85                  90                  95
ATC ATG CTG CGC GGC CTT CCC ATC ACC ATC ACA GAG AGC GAT ATT CGA       451
Ile Met Leu Arg Gly Leu Pro Ile Thr Ile Thr Glu Ser Asp Ile Arg
100                 105                 110                 115
GAA ATG ATG GAG TCC TTC GAA GGC CCT CAG CCT GCG GAT GTG AGG CTG       499
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ATG AAG AGG AAA ACA GGT GAG AGC TTG CTT AGT TCC TGATATTATT            545
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            135                 140
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SEQ ID NO:1
SEQUENCE LENGTH: 2660
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human

CELL TYPE: leukocyte
SEQUENCE:

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Arg Arg Arg Asp Ser Asp Tyr Lys Arg Ser Ser Asp Asp Arg Arg Gly
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GAT AGA TAT GAT GAC TAC CGA GAC TAT GAC AGT CCA GAG AGA GAG CGT     310
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GAC TAT GGT GAG CAC GAC TAT AGG CAT GAC ATC AGT GAC GAG AGG GAG     406
Asp Tyr Gly Glu His Asp Tyr Arg His Asp Ile Ser Asp Glu Arg Glu
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AGC AAG ACC ATC ATG CTG CGC GGC CTT CCC ATC ACC ATC ACA GAG AGC     454
Ser Lys Thr Ile Met Leu Arg Gly Leu Pro Ile Thr Ile Thr Glu Ser
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GAT ATT CGA GAA ATG ATG GAG TCC TTC GAA GGC CCT CAG CCT GCG GAT     502
Asp Ile Arg Glu Met Met Glu Ser Phe Glu Gly Pro Gln Pro Ala Asp
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SEQ ID NO:2
SEQUENCE LENGTH: 155
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CACTTATAAA ATGTTAGGGC TTAATATTAT TCATAGATCG AGGATAGTTT CATTCTTAGT 60
CGCCTCCTTA GTCACTCTTC CTATACCAAT CTGAGACCAT TTTACAATTT AGAAAAGACA 120
AATAACTGGT TGGGTTACTT GATAGTATAA TAACC 155

SEQ ID NO:3
SEQUENCE LENGTH: 305
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA

ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TCATGAAGTG AAGCCAACTG TTTAGACTAG AATGTTATGA GATTAAACCC ACNNNNNNTT 60
ATTCATAGAC ATAAACCCTC ATTTTAATTA GTGGATCTGG ATTTTTGTCA TATGTGGAAT 120
CATAATTTAA ACAAAATCAA CTAAGATGAT CCAAGTTCCA CACAACTGCA CTTCAATATT 180
CAAGTCGGTG TGAAGATGCC TGACTACTGC GTCACAAGAT TCTGAGCTGT CGTAAAAAGC 240
CTGGCTCGTG GTTTCTATTT ATAGTGTACA CATGTTGGGT TATAATCACA AACCTGGAAC 300
TCTGT 305

SEQ ID NO:4
SEQUENCE LENGTH: 278
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
GAAGGAGAAT ATGAAGAGGT TAGAAAAGNT CNGGNTTCTG TTGGTGAAAT GAAGGATGAA 60
GGGGAAGAGA CATTAAATTA TCCTGATACT ACCATTGACT TGTCTCACCT TCAACCCCAA 120
AGGTCCATCC AGAAATTGGC TTCAAAAGAG GAATCTTCTA ATTCTAGTGA CAGTAAATCA 180
CAGAGCCGGA GACATTTGTC AGCCAAGGAA AGAAGGGAAA TGAAAAAGAA AAAACTTCCA 240
AGTGACTCAG GAGATTTAGA AGCGTTAGAG GGAAAGGA 278

SEQ ID NO:5
SEQUENCE LENGTH: 135
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TTCTGACAAT GAGTAAGAAG AAAGAGGGTC TTGCCCTTTG GTTATTAAGA TTTATCATAG 60
AGCAATAATA ASTAAATCGG TGTTATACCA GCACAGAGAT TAGACAAATA AACCAAGGGA 120
CTGGACTAAA TAAGC 135

SEQ ID NO:6
SEQUENCE LENGTH: 197
SEQUENCE TYPE: nucleic acid

STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
ATGGTACCCA GTTTCAAATT AACATGGTTA TTTTACTTGT GTTCCCAAAT TTAACATTAG 60
GGAATTTTTG GTTGTGGGTC TGTTATCACT AGAAAAATAT ATATATTGGT GCTGAAGATA 120
ATTTTGAGAT AATTAGACAA GACAGTTTAG CATTTACAAG AACAAGTTTG GCAGTTGAAG 180
AATCTATTTA TATGACT 197

SEQ ID NO:7
SEQUENCE LENGTH: 137
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CCACCGCACC TGGCTGATGC TTTTCTATCT GACTTCTTTC AGAGGACCCT GAAAGACACT 60
AAGTGGAATC TTTCCTTGAA GTCTTCCAAG CTAAAACAAT TCTCTGGAAA GATCACCTCT 120
GTTCAGTCCT GGTCTCT 137

SEQ ID NO:8
SEQUENCE LENGTH: 274
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CGTTTACAGA TTCTCTTGCG GCTGGCGGTG GAACTACAAA GGGATCGGTG CCTATATCAC 60
AATACCAAAC TTGATAATAA TCTAGATTCT GTGTYTCTGC TTATAGACCA TGTTTGTAGT 120
AGGTAAGAGG AAAACTTCCT ATATTCTGAA ACAGCCTAAC ATTTTACAAA ATTTTAGTTT 180
TCTTTTTTAG AGTCTTATCC TGTAGCTATA TAACAGTTCA TGTCTGATTT AGCATTTGTT 240
CACGAGTAAA GCTGGAACTA TGAAAATTGA AAAT 274

SEQ ID NO:9
SEQUENCE LENGTH: 171

SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
GATTAGGTGA CCTTCCTTGA ARAGCCACGG GTTTCCCATA TCGAAATGCT ATTCATTACC 60
CGAGTCACCT ANGTTCTTAC AAAGGAAGCG AGAAAATTGC TTTTGTTGGG CCATGCCCCT 120
TTTGCANAGG TTCCTAAGTA TAGTCGCCAN AATTTTTTTA ATGGCCTAAA G 171

SEQ ID NO:10
SEQUENCE LENGTH: 161
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
AGGGGCGCTT GTTCTGCTCT CAGCAGATTG GTTACACGCG TCAGGTGGTG GCGATGACTT 60
AATTCCTAGC CCAAGAAGAA TATAATGTTA AAACTGGTTA TGTAATTTTT GTGCCTCTCC 120
TTTTTAATGC AGTATTTAGT TCAGATGTTG GCGATTTTTC A 161

SEQ ID NO:11
SEQUENCE LENGTH: 323
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TATAAGGWGG GAACCTTACT ATCTCTAATG ACCTTACTGA TGCTGACTTT AATACTCTGT 60
GAAGGTTAGA GTTCAGTGAA TGTTACCTAG AAACAGCCCC GGCTGTGGAA TACTTTATTC 120
TTAGCCCTAT ATTTGGGGTT TGGATGTCCA CTGTGCTGGT TCCCAGAGAT AGTAAGGGGA 180
TGAGAGTATT GGTTACATCT CCTGACCCAC ATACTTAAGA TCCAGATGAA CAAGACAGTT 240
TTCACTCCTG CTTGGTAGAA CCTATTTGYK SHAGGAAACA GYTCCTAAAG AATGGTTCTA 300
GCCAGACCCT GTCGYTACCA GAA 323

SEQ ID NO:12

SEQUENCE LENGTH: 138
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
AGTATGACAA ATAGTTTCTG CCTGATTGGT GAGATTTGGG ATGGGCCCCC ACTTTGTTTC 60
TCTTTCTGCA TAAAAATTTC AACATTTTTA CAAAATTTTC AAAAACTTCT CCTCAGTCTG 120
TACATCTTTG TTAATCAG 138

SEQ ID NO:13
SEQUENCE LENGTH: 244
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TACTCTTCAA CCATGATTTT TCTCTGATGG CCTGTGTGAA CAGATTAATG GTGTCCATCT 60
AATTCCTTCC CCACTGGGGG AAAGCAAATC ATCAGGCCCA TTGCAAAAAC TGCTCTTGGT 120
TGAGCTTCCT GCCTTAAATC ATACCCACAG TGAATGGCGT CCCTTTATCA CCGCTAATGA 180
CTCTGACATC TCTCTCCACT CACATGTGAG CCTCCTCAGC TCTCGANAAA CAAGTCNGTC 240
TCGG 244

SEQ ID NO:14
SEQUENCE LENGTH: 135
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TGATCCCCAC AATTTCTTGT GATTGGTGAG GAACTATAAA TGACTCCCAT CCAAGCTTAT 60
ACCAGAAAAA AGGAGCACAT TTTCTACAAA TTATATCATT TTTAATCCAT TACCACATTA 120
TTTTAGGGGA ACTAC 135

SEQ ID NO:15

SEQUENCE LENGTH: 258
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TCTCAGAAAA CTCCAGATCA AATGAGATGA GTATGGTGNN NAGGGCTGGC AATTAGAGGA 60
TACTCTCCAA TGGTGATGAA GGGAGATGTC TGGGGGAAAT CCAGCAGGAT GTTGATTTAG 120
TATGTACACA GTGAGAGGAT ACTTGTAGAG AACCTAGAAT CTTCTCTGAA TGTGACGGGC 180
CCTCAGAGAT AATTGTTAAC AGATAAGTGG ATGATTAAAT ACACTTCCTC CAGTAGGCTA 240
GATGTTAAGA CGGAGATC 258

SEQ ID NO:16
SEQUENCE LENGTH: 219
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CTGAGAGGAG CCATGTATAC AAACCACTTT TTCTAACATG GTCTTTATTA AACTTTGAAT 60
ATAAGTACAC CTGCTCGAAG TGTTCATCTA TATTATTTAA GAACAAGCAA CTGTAAAACA 120
GTAAAATCAC AAAAGGTAAG TTGTTGGAAG ACAACAAAAA AGAATTACTA TATCTGATCC 180
TGCGTGTTTA TTTTAGAATC TGTTAATAGG CCTACAGCT 219

SEQ ID NO:17
SEQUENCE LENGTH: 191
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
ACAGTGAGTG TGGCTGAAAC CTAAGCTGAA GGAAGGGAGG AGCAGGCACT GCCATGAGGG 60
GTCCCTGGAC AGAAACTCTT CAGCAGGCCT TGAAGTTTAG TTCAGGGGCT ACATGGAATA 120
CCACTATTTA GCACACAGGT GTGATCTGAG GTGAGGGACT ACCTTTTCGA TCTTGGTTTT 180
CTCATTTATT T 191

SEQ ID NO:18
SEQUENCE LENGTH: 148
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CTGGAGGTGA AGGGAAGGAA AGAAAGGAAA AACTATCTAC CTGGCAGGAA AAGAGATAAG 60
CTCCCAAGAA CACCAAAGCA GATGATGAGT CTAGCTCTAC CCAGCCTTCC TCCCCACGAA 120
TCCAGATCAT AGTAAGAAAC TCTGGGCT 148

SEQ ID NO:19
SEQUENCE LENGTH: 306
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CCACCACCAG AAATGAACAA AAAGCATTTT ACCTAAAAAT ACACCAGCAA AATGTACTCA 60
GCTTCAATCA CAAATACGAC TGCTTAAAAC CGCAGAAATT TCCTCAACAC TCAGCCTTTA 120
TCACTCAGCT GGATTTTTTC CTTCAACAAT CACTACTCCA AGCATTGGGG AACACAACTT 180
TTAATCATAC TCCAGTCGTT TCACAATGCA TTCTAATAGC AGCGGGATCA GAACAGTACT 240
GCATTTACTT GCCAACAGAA CAGACAGACC TGAAGTCAAG ACAACTGCAT TCTCTGTGAA 300
GTCTGT 306

SEQ ID NO:20
SEQUENCE LENGTH: 357
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
GTAGCATTTT GGCAGAACCA TTGTTAATTA AAGGGACTTY TGGACCGCAA CYTTAATGTA 60
CCAGATTATT GAGCRGCCCA ATGAATGCTT CATTCTCATT GTTTAAGGTG CTGCTTTGAT 120

TTTTTTTTCA ATTCTTTGTA CTATTTTTTA TTTTTTGGAG AGGCACATCC CCAAATTTGG 180
ATGAGGTATT TGTTGATAAA TAATTCATCA ATTTCCACAA TGCAGACAAA AATGTCTGCC 240
CAGAGTGGAA AAATAAAACA AGGGGGAGAA GAGTTTGAGT AACGGAGAAG TTCTGTGGAA 300
TCCTAGTGAC AAAAGTTGAG AAACTACCTT TAAATAAGAC AGTGAGGTAA CAAATGT 357

SEQ ID NO:21
SEQUENCE LENGTH: 219
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TGGAATAGCC AGGAGAATTC TGGAAAAGTA GAATAATGAG GTAGGGCTTC CCTTCGCTAT 60
TTTGAAGTGC AGATTACACT ATGTAAAACC ATTAGGAACT GGCACGTGAA TAGACAGATC 120
AATAGTTAAT AGCTGTATTA GCCAGAAAAT GGTGTAAGGA CAACAGGCTA ACTAACCCTG 180
TCACTTGTTA TGCTAAAATT AAGTCTAGAT AGAGTCCTC 219

SEQ ID NO:22
SEQUENCE LENGTH: 251
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TGAAAGGGGA ATAGAAGCAC AAGAGTCAGT AATCAATAAC AAACAACTCA AGGTGCTCCT 60
TCCTTACACT GGTGTTCCCC AAAGTGAGGT GAATTGCCAG CCACTGGGAG TCAGGGCCAG 120
TTACATAAGA CATTCTCGGT AAGCCCCCTT TGGGTATCCC AAATAAGGAC TGGGGTGGGT 180
TTATGTGTAG TCCATTATTA ACAACTAAAC GAACAAACCT AGTGAATTGC AATAAATTCA 240
CACCAACAGA A 251

SEQ ID NO:23
SEQUENCE LENGTH: 233
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human

CELL TYPE: leukocyte
SEQUENCE:
GTTGAAAGAG TCCTTGGAAG GCTTTTAGAC CAAACCCCTC TGCATGCTCA ARCCTTGGGT 60
ACAGGATTTC TAAGAAGTGG AACAGTCTCC AGGGGTGTGG ARCTCATCGC TCAAGGCAGG 120
TTATCTTATC TGAATAATTT TGTCTGTTGA CTATTGGGAT AGTTCTCCTT CAGATGAGCT 180
GAAATTTTCT CCATAGCTTC CTCTATTAAA CCCAATTCCA CTTCTCAGGG TCA 233

SEQ ID NO:24
SEQUENCE LENGTH: 176
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CAAAAGCGCT GAAGTTAAGC ATTAATACGC CAGATTCATG ATTTATGATC AGTATCCAAA 60
ACTCCAACTA CAAACAATGC AAAGTAGTGC TCCTCAGTAT TATTTTTGCA ATTGTTAGTA 120
ATGTTAAGCA TCAAGGAAAA TAAAACACAT CATTGCACAT TACAGCCGCA AAAAAC 176

SEQ ID NO:25
SEQUENCE LENGTH: 241
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
AGAGAGTAAA GCAAGCTATT TTGACAGCAA CCTAATAACA GCTGTCTTCT TCCACTTCTT 60
GGCTAACTCA TCCCCCAGAT AGCCTTCTTT TCTCTTATCA ATTCCCTGTT GCAACAATAA 120
TAAATGCCAC ACCTGATGGA GTCATTAGGC ACTTTCCTAG TGACAAGTGC CTAGGACAGA 180
GGAGAAAACA AAGAAACACT GACAACCACT GAAAACTGAC ATATCAGGCC AGGCATGTCA 240
C 241

SEQ ID NO:26
SEQUENCE LENGTH: 217
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE

ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
GCTGGAGAGG TGGTGATGTT GCTGAATAAT TGCTTTTTAA AGCTGGAGGG GACTTCCAAG 60
AGTCTCTCAT TTAAGAARAA AAATTAAAGA CATAATTGGT AACGGTTTTG ACTGCTGCAG 120
AGGCAACACT TTGCTCACAA TCCTACAGAT CTACTTCACC TGTAACTACA ATTTTCCTGA 180
AGACATAGAA GAAAAATCAA TTGTTCTAAT CCATATG 217

SEQ ID NO:27
SEQUENCE LENGTH: 233
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
AATCTTAGCA TAATGCTTCC TGGGAAATTC TGAAATTGAT TCCATTTCTG CCGTTACAAA 60
CACACACGAA GTTCCTAGTT CACTGGGACT TCCTGATTTG TTCTTTTAGC TTGCTCCTTC 120
TCACCTAGAA GCTCTGTTTA TTTCTGAGCA ACCCTGGGGC TTGTCTCATA GGACAGGATT 180
TATTTATCTC ATCAAGGCTG AGTGTGCCTT AGGAAGTCAT AAACATAAAA AGA 233

SEQ ID NO:28
SEQUENCE LENGTH: 228
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
TATAGACAGG GTAGGGACGA TTAGCCCCTC GACAACTTTT CACAAATATA CACACGTTTA 60
ACTACCTCTC AGGTCATGAT AAAGACCGGC CGGGCAGAAA CACTGTAATC CCAGCTACTC 120
GGGAGCCTGA GGCATGAGAA TCACTTGAAC CTGGGAGGTG GAGGTTGCCA TGAGCCGAGA 180
TCACGCCATT GCACTACAGC CTTGGCGACA AGAGTGAAAC TCCATCTG 228

SEQ ID NO:29
SEQUENCE LENGTH: 298
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA

ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
GCTTATGATT ACAAACATCC CTCATATGAA AATCTCAGCA TTTNCTGGCT GCTGCCTTCA 60
ATCGCTTTTT CTGAAATAGG TATCCCTTGA TGTCGACTAT TTGATTTCAG CCAGTCGTTT 120
CTCTCTGGCA GTGCTCCCTG CAAATGTGTC CTTTCAAGAA AACAAAACCT GCAAGTGGCT 180
TGTAATGTAC CATGACCTTA TCATGTGAAG GACAAATGGC TCTTGTGCTT ATTAGATAGC 240
AGATGAACTG ATGAACTGAA TTCTTGGTCT GAAGCTTTGA TAAGGTCAGA TGTCTTTG 298

SEQ ID NO:30
SEQUENCE LENGTH: 291
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
ACTTCGAAGG GAAAAAGAGG AAGGAAAAGG ACTGTTAATA AAATAACAAA GGCAGCAATC 60
AGAATGAACC AGAGCCAGGA CAGCGTAAAG GCTAGGTTCA CAGTGAGATG AAAGAACCTG 120
AAAACAAGTT TAAAACTCAA AAGAGGATTA TTCTCAAGTT ATACTACAGT GAAAAAACAT 180
GGAAAAACAC AAAAAGGACA GGCAATAAGG CACAGGCATA CATACAAGGC AAATTGTAAC 240
ACAATATTTA CTTGCAAAAG AGCCCACAGA GACATGTCAA TGAAGTCATA G 291

SEQ ID NO:31
SEQUENCE LENGTH: 869
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
MOLECULE TYPE: cDNA
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:
CGCGTCCGGT GCCTGGCTGC AGTAGCAGCG GCATCTCCCT TGCACAGTTC TCCTCCTCGG 60
CCTGCCCAAG AGTCCACCAG GCCATGGACG CAGTGGCTGT GTATCATGGC AAAATCAGCA 120
GGGAAACCGG CGAGAAGCTC CTGCTTGCCA CTGGGCTGGA TGGCAGCTAT TTGCTGAGGG 180
ACAGCGAGAG CGTGCCAGGC GTGTACTGCC TATGTGTGCT GTATCACGGT TACATTTATA 240
CATACCGAGT GTCCCAGACA GAAACAGGTT CTTGGAGTGC TGAGACAGCA CCTGGGGTAC 300
ATAAAAGATA TTTCCGGAAA ATAAAAAATC TCATTTCAGC ATTTCAGAAG CCAGATCAAG 360
GCATTGTAAT ACCTCTGCAG TATCCAGTTG AGAAGAAGTC CTCAGCTAGA AGTACACAAG 420
GTACTACAGG GATAAGAGAA GATCCTGATG TCTGCCTGAA AGCCCCATGA AGAAAAATAA 480

AACACCTTGT ACTTTATTTT CTATAATTTA AATATATGCT AAGTCTTATA TATTGTAGAT 540
AATACAGTTC GGTGAGCTAC AAATGCATTT CTAAAGCCAT TGTAGTCCTG TAATGGAAGC 600
ATCTAGCATG TCGTCAAAGC TGAAATGGAC TTTTGTACAT AGTGAGGAGC TTTGAAACGA 660
GGATTGGGAA AAAGTAATTC CGTAGGTTAT TTTCAGTTAT TATATTTACA AATGGGAAAC 720
AAAAGGATAA TGAATACTTT ATAAAGGAWT AATGTCAATT CTTGCCAAAT ATAAATAAAA 780
ATAATCCTCA GTTTTTGTGA AAAGCTCCAT TTTTAGTGAA ATATATTTTA TAGCTACTAA 840
TTTTAAAATG TCTGCTGATG TATGTGGAA 869

SEQ ID NO:32
SEQUENCE LENGTH: 143
SEQUENCE TYPE: amino acid
TOPOLOGY: linear
MOLECULAR TYPE: protein
ORIGINAL SOURCE
ORGANISM: human
CELL TYPE: leukocyte
SEQUENCE:

Met Gly Ser Asp Lys Arg Val Ser Arg Thr Glu Arg Ser Gly Arg Tyr
1 5 10 15
Gly Ser Ile Ile Asp Arg Asp Asp Arg Asp Glu Arg Glu Ser Arg Ser
20 25 30
Arg Arg Arg Asp Ser Asp Tyr Lys Arg Ser Ser Asp Asp Arg Arg Gly
35 40 45
Asp Arg Tyr Asp Asp Tyr Arg Asp Tyr Asp Ser Pro Glu Arg Glu Arg
50 55 60
Glu Arg Arg Asn Ser Asp Arg Ser Glu Asp Gly Tyr His Ser Asp Gly
65 70 75 80
Asp Tyr Gly Glu His Asp Tyr Arg His Asp Ile Ser Asp Glu Arg Glu
85 90 95
Ser Lys Thr Ile Met Leu Arg Gly Leu Pro Ile Thr Ile Thr Glu Ser
100 105 110
Asp Ile Arg Glu Met Met Glu Ser Phe Glu Gly Pro Gln Pro Ala Asp
115 120 125
Val Arg Leu Met Lys Arg Lys Thr Gly Glu Ser Leu Leu Ser Ser
130 135 140 143

SEQ ID NO:33
SEQUENCE LENGTH: 26
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GGGCTTAATA TTATTCATAG ATCGAG

SEQ ID NO:34
SEQUENCE LENGTH: 26
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTTATTATAC TATCAAGTAA CCCAAC

SEQ ID NO:35
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTGGATCTGG ATTTTTGTCA TATGT

SEQ ID NO:36
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTTTGTGATT ATAACCCAAC ATGTG

SEQ ID NO:37
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAAGGGGAAG AGACATTAAA TTATC

SEQ ID NO:38
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:

GCTTCTAAAT CTCCTGAGTC ACTT

SEQ ID NO:39
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACAATGAGT AAGAAGAAAG AGGG

SEQ ID NO:40
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTCCAGTCCC TTGGTTTATT TGTC

SEQ ID NO:41
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GGTACCCAGT TTCAAATTAA CATGG

SEQ ID NO:42
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GATTCTTCAA CTGCCAAACT TGTTC

SEQ ID NO:43
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA

SEQUENCE:
GCTGATGCTT TTCTATCTGA CTTC

SEQ ID NO:44
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACCAGGACT GAACAGAGGT GA

SEQ ID NO:45
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCTTATAGAC CATGTTTGTA GTAGG

OSEQ ID NO:46
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTGAACAAAT GCTAAATCAG ACATG

SEQ ID NO:47
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCCACGGGTT TCCCATATCG AA

SEQ ID NO:48
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear

MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACTATACTT AGGAACCTCT GCAA

SEQ ID NO:49
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTTCTGCTCT CAGCAGATTG GTTA

SEQ ID NO:50
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCCAACATCT GAACTAAATA CTGC

SEQ ID NO:51
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTTCAGTGAA TGTTACCTAG AAACA

SEQ ID NO:52
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GGAGTGAAAA CTGTCTTGTT CATC

SEQ ID NO:53
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single

TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTATGACAAA TAGTTTCTGC CTGAT

SEQ ID NO:54
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GATTAACAAA GATGTACAGA CTGAG

SEQ ID NO:55
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGACAGCAT TCAGATATAG ACGG

SEQ ID NO:56
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCGTGGAATC AAATGGAGTG GC

SEQ ID NO:57
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GATGGCCTGT GTGAACAGAT TAAT

SEQ ID NO:58
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid

STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGAGAGATG TCAGAGTCAT TAGC

SEQ ID NO:59
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GATCCCCACA ATTTCTTGTG ATTG

SEQ ID NO:60
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTTCCCCTAA AATAATGTGG TAATG

SEQ ID NO:61
SEQUENCE LENGTH: 23
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGGATACTC TCCAATGGTG ATG

SEQ ID NO:62
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTCTTAACAT CTAGCCTACT GGAG

SEQ ID NO:63
SEQUENCE LENGTH: 24

SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGAGGAGCC ATGTATACAA ACCA

SEQ ID NO:64
SEQUENCE LENGTH: 26
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCACGCAGGA TCAGATATAG TAATTC

SEQ ID NO:65
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCTGAAACCT AAGCTGAAGGAAGG

SEQ ID NO:66
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTCCCTCACC TCAGATCACA CC

SEQ ID NO:67
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCTATCTACC TGGCAGGAAA AGAG

SEQ ID NO:68

SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGTTTCTTA CTATGATCTG GATTC

SEQ ID NO:69
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCAAAATGTA CTCAGCTTCA ATCAC

SEQ ID NO:70
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTAAATGCAG TACTGTTCTG ATCC

SEQ ID NO:71
SEQUENCE LENGTH: 26
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAATGCTTCA TTCTCATTGT TTAAGG

SEQ ID NO:72
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTCACTAGGA TTCCACAGAA CTTC

SEQ ID NO:73
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGGTAGGGC TTCCCTTCGC TA

SEQ ID NO:74
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCATAACAAG TGACAGGGTT AGTTA

SEQ ID NO:75
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GGTGCTCCTT CCTTACACTG GT

SEQ ID NO:76
SEQUENCE LENGTH: 23
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACTACACAT AAACCCACCC CAG

SEQ ID NO:77
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GGGTACAGGA TTTCTAAGAA GTGG

SEQ ID NO:78
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GGAGAAAATT TCAGCTCATC TGAAG

SEQ ID NO:79
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCTGAAGTTA AGCATTAATA CGCC

SEQ ID NO:80
SEQUENCE LENGTH: 23
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCGGCTGTAA TGTGCAATGA TGT

SEQ ID NO:81
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACAGCAACC TAATAACAGC TGTC

SEQ ID NO:82
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:

GTCCTAGGCA CTTGTCACTA GG

SEQ ID NO:83
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAGGGGACTT CCAAGAGTCT CT

SEQ ID NO:84
SEQUENCE LENGTH: 25
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTCTTCAGGA AAATTGTAGT TACAG

SEQ ID NO:85
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTTACAAACA CACACGAAGT TCCT

SEQ ID NO:86
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACTTCCTAA GGCACACTCA GC

SEQ ID NO:87
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA

SEQUENCE:
GTTTAACTAC CTCTCAGGTC ATGA

SEQ ID NO:88
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GTCGCCAAGG CTGTAGTGCA AT

SEQ ID NO:89
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAAATAGGTA TCCCTTGATG TCGA

SEQ ID NO:90
SEQUENCE LENGTH: 24
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GACCAAGAAT TCAGTTCATC AGTT

SEQ ID NO:91
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GAATGAACCA GAGCCAGGAC AG

SEQ ID NO:92
SEQUENCE LENGTH: 22
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear

MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
GCCTTGTATG TATGCCTGTG CC

SEQ ID NO:93
SEQUENCE LENGTH: 21
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
AAGAGTCCAC CAGGCCATGG A

SEQ ID NO:94
SEQUENCE LENGTH: 23
SEQUENCE TYPE: nucleic acid
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE TYPE: other nucleic acid, synthetic DNA
SEQUENCE:
TACCTTGTGT ACTTCTAGCT GAG

Claims

1. A DNA related to IgA nephropathy gene, comprising the nucleotide sequence represented by SEQ ID NO:1 to NO:31.

2. A DNA which hybridizes with the DNA comprising the nucleotide sequence according to claim 1 under stringent conditions.

3. An oligonucleotide, comprising a part of the nucleotide sequence of the DNA according to claims 1 and 2.

4. An oligonucleotide, comprising a part of the nucleotide sequence complementary to the DNA according to claims 1 and 2.

5. A method for detecting mRNA of an IgA nephropathy-related gene, comprising using the oligonucleotide according to claims 3 and 4.

6. An IgA nephropathy diagnostic agent, comprising the oligonucleotide according to claims 3 and 4.

7. A method for inhibiting transcription of an IgA nephropathy-related gene or translation of mRNA of an IgA nephropathy-related gene, comprising using the oligonucleotide according to claims 3 and 4.

8. An IgA nephropathy therapeutic agent, comprising the oligonucleotide according to claims 3 and 4.

9. A method for isolating an IgA nephropathy gene from leukocytes of a patient with IgA nephropathy, comprising conducting a differential display method.

10. A protein comprising the amino acid sequence represented by SEQ ID NO:32.

11. A DNA encoding the protein according to claim 10.

12. The DNA according to claim 11, comprising the nucleotide sequence represented by SEQ ID NO:1.

13. A DNA which hybridizes with the DNA comprising the nucleotide sequence according to claim 12 under stringent conditions.

14. A recombinant DNA, comprising the DNA according to claims 11 to 13 and a vector.

15. A transformant obtained by introducing the recombinant DNA according to claim 14 into a host cell.

16. A method for producing the protein according to claim 10, comprising the steps of culturing the transformant according to claim 15 in a medium to produce and accumulate a protein in the culture; and recovering the protein from the resulting culture.

17. An antibody which specifically reacts with the protein according to claim 10.

18. A method for immunologically detecting the protein, comprising using the antibody according to claim 17.

19. An IgA nephropathy diagnostic agent, comprising the antibody according to claim 17.

20. An IgA nephropathy therapeutic agent, comprising the antibody according to claim 17.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP97/04468

A. CLASSIFICATION OF SUBJECT MATTER
Int. Cl^6 C12N15/12, C07K14/47, C12Q1/68, A61K38/17, C12P21/02, G01N33/53, G01N33/577
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int. Cl^6 C12N15/12, C07K14/47, C12Q1/68, A61K38/17, C12P21/02, G01N33/53, G01N33/577

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
BIOSIS(DIALOG), WPI(DIALOG), GenBank/EMBL/DDBJ(GENETYX)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X/Y	Plant Physiol., Vol. 106, (1994), Newman T. et al.,; "Genes galore: a summary of methods for accessing results from large-scale partial sequencing of anonymous Arabidopsis cDNA clones.", see p. 1241-1255	3/4
A	Clin. Exp. Immunol., Vol. 103, (1996), H. Ichinose et al., "Detection of cytokine mRNA-expressing cells in peripheral blood of patients with IgA nephropathy using non-radioactive in situ hybridization.", see p. 125-132	1 - 20
A	Kidny International, Vol. 2, (1996), Hunley T.E. et al.,; "Angiotensin converting enzyme gene polymorphism: Potential silencer motif and impact on progression in IgA nephropathy", see p. 571-577	1 - 20

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
March 3, 1998 (03. 03. 98)	March 17, 1998 (17. 03. 98)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP97/04468

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FEBS Letters, Vol. 351, (1994), T. Ito et al., "Fluorescent differential display: arbitrarily primed RT-PCR finger-printing on an automated DNA Sequencer.", see p. 231-236	9

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